Serial No.: 09/529,232

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claim 1. (currently amended) A thrombin inhibitor of formula (I) or a pharmaceutically acceptable salt thereof:

AS-Z-P (I)

wherein

AS represents a S subsite blocking segment;

P represents a fibrinogen recognition exosite blocking segment; and

Z represents a S' subsite blocking segment which links AS and P, said S' subsite blocking segment having the following sequence:

Xaa-Gly-Yaa-Gly-βAla

wherein Xaa is a residue selected from the group of residue consisting of glycine, L-alanine, D-alanine, 2-aminoisobutyric acid, L-α-aminobutyric acid, D-α-aminobutyric acid, L-norvaline, D-norvaline, L-norleucine, D-norleucine, L-cysteine, L-penicillamine, D-penicillamine, L-methionine, D-methionine, L-valine, D-valine, L-tert-butylglycine, D-tert-butylglycine, L-isoleucine, D-isoleucine, L-leucine, D-leucine, cyclohexylglycine, L-β-cyclohexylalanine, D-β-cyclohexylalanine, L-phenylglycine, D-phenylglycine, L-phenylalanine, D-phenylalanine, L-homophenylalanine, D-homophenylalanine, L-histidine, D-histidine, L-tryptophan, D-tryptophan, L-β-(2-thienyl)-alanine, and D-β-(2-thienyl)-alanine;

Yaa is selected from the group of residue consisting of glycine, L-alanine, D-alanine, 2-aminoisobutyric acid, L-α-aminobutyric acid, D-α-aminobutyric acid, L-norvaline, D-norvaline, L-norleucine, D-norleucine, L-cysteine, L-penicillamine, D-penicillamine, L-methionine, D-methionine, L-valine, D-valine, L-tert-butylglycine, D-tert-butylglycine, L-isoleucine, D-isoleucine, L-leucine, D-leucine, cyclohexylglycine, L-β-cyclohexylalanine, D-β-cyclohexylalanine, L-phenylglycine, D-phenylglycine, L-phenylalanine, D-phenylalanine, homophenylalanine, histidine, L-tryptophan, D-tryptophan, L-β-(2-thienyl)-alanine, and D-β-(2-thienyl)-alanine.

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Claim 2. (currently amended) The thrombin inhibitor of claim 1, wherein AS has the following sequence:

Bbs-Arg-(D-Pip),

wherein Bbs and D-Pip represent 4-tert-butylbenzenesulfonyl and D-pipecolic acid, respectively.

Claim 3. (currently amended) The thrombin inhibitor of claim 1, wherein P has the following sequence:

Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH,

wherein Cha represents β-cyclohexyl-alanine.

Claim 4. (currently amended) The thrombin inhibitor of claim 2, wherein P has the following sequence:

Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH,

wherein Cha represents β-cyclohexyl-alanine.

Claim 5. (currently amended) The inhibitor of claim 1, wherein said inhibitor is selected from the group consisting of:

1) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Ala)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH; (SEQ ID NO:3)

2) Bbs-Arg-(D-Pip)-αAbu-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

3) Bbs-Arg-(D-Pip)-Gly-Gly-(D-αAbu)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

4) Bbs-Arg-(D-Pip)-Nva-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

5) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Nva)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

6) Bbs-Arg-(D-Pip)-Nle-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

7) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Nle)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

8) Bbs-Arg-(D-Pip)-Met-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

9) Bbs-Arg-(D-Pip)-Val-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

10) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Val)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

11) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Tbg)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

12) Bbs-Arg-(D-Pip)-Ile-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

13) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Ile)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

14) Bbs-Arg-(D-Pip)-Leu-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

15) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Leu)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

16) Bbs-Arg-(D-Pip)-Chg-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

17) Bbs-Arg-(D-Pip)-Cha-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

18) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Phg)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

19) Bbs-Arg-(D-Pip)-Phe-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

20) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Phe)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

21) Bbs-Arg-(D-Pip)-Hph-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

22) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Hph)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

23) Bbs-Arg-(D-Pip)-His-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

and

24) Bbs-Arg-(D-Pip)-Thi-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH

(SEQ ID NO:3).

Claim 6. (currently amended) The inhibitor of claim 1, wherein said inhibitor is selected from the group consisting of:

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1) Bbs-Arg-(D-Pip)-Nle-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

2) Bbs-Arg-(D-Pip)-Gly-Gly-(D-Phg)-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH;

(SEQ ID NO:3)

and

3) Bbs-Arg-(D-Pip)-Thi-Gly-Gly-Gly-βAla-Asp-Tyr-Glu-Pro-Ile-Pro-Glu-Glu-Ala-Cha-(D-Glu)-OH

(SEQ ID NO:3).

Claim 7. (Deleted)

Claim 8. (Deleted)

Claim 9. (currently amended) A pharmaceutical composition for treating vascular disease, said composition comprising a therapeutically effective amount of an inhibitor as defined in claim 1, and a pharmaceutically acceptable carrier.

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Claim 10. (currently amended) A pharmaceutically acceptable composition for treating vascular disease in a mammal, comprising an inhibitor as defined in claim 1, a thrombolytic agent and a pharmaceutically acceptable carrier.

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Supprimé : or preventing

Supprimé : a compound

Claim 11. (Currently amended) The composition according to claim 10, wherein said thrombolytic agent is tissue plasminogen activator.

Supprimé : combination

Claim 12. (Currently amended) The composition according to claim 10, wherein said mammal is a human.

Supprimé : combination

Claim 13. (Currently amended) A method for the treatment of vascular diseases of a mammal comprising the administration of an effective amount of a composition according to claim 10.

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Claim 14. (Original) The method according to claim 13, wherein said mammal is a human.